

REMARKS

Applicant intends this response to be a complete response to the Examiner's **10 June 2008** Final Office Action. Applicant has labeled the paragraphs in his response to correspond to the paragraph labeling in the Office Action for the convenience of the Examiner.

Preliminary Remarks

It is important that the examiner be aware that coronary plaques that are located proximally (close to the coronary ostium or left main coronary artery) confer higher levels of risk than plaques located distally (distal branches of the left anterior descending, right coronary, or left circumflex arteries). The rationale behind this assertion is two-fold. First, proximal plaques hemodynamically experience a higher degree of shear stress, which is an important factor in plaque rupture and other complications. Second, occlusive complications (rupture or vasospasm) caused by a proximal plaque would place a larger area of heart muscle in danger than a distal plaque would. Therefore, cardiac risk assessment can be improved by additionally weighing the risk of a plaque (calcification) based on its location.

Similarly, the presence of an area of very high density immediately adjacent to an area of very low density (abrupt change in regional coronary elasticity) is indicative of a soft plaque being adjacent to a hard plaque; this co-existence of a hard plaque next to soft plaque confers higher risk than existence of merely a hard plaque or a soft plaque.

Finally, for the purpose of monitoring changes in risk over time, even if the total calcium score (as taught by prior art) does not change, but the features as taught by Naghavi et al. in this patent application, for example, changes in heterogeneity, shape, texture, and changes in density gradient (abrupt transition), do change, this situation could result in a different risk assessment that otherwise could have been missed.

The Examiner states as follows:

This action is in response to communications filed 20 February 2008. The revised abstract has been acknowledged and entered. Claims 1 and 17 have been amended to include "defining an *anatomical* distribution of the areas of calcification within the located area," but this feature is not supported by applicant's specification; therefore, new grounds of rejection under the first paragraph of 35 U.S.C. 112 are presented herein.

Applicants acknowledge these statements.

Response to Arguments

The Examiner states as follows:

Applicant's arguments have been fully considered but they are not persuasive and/or are moot in view of new grounds of rejection.

Applicant asserts that Bu et al., in determining an overall calcium score, teaches away from the claimed invention. Examiner disagrees. The claims as amended specify that a distribution of calcification is determined (including an anatomical distribution), and Strauss et al. is relied upon to establish that this technique is well known to artisans in the coronary calcification imaging arts. Unger

et al. (US 7,105,828) is additionally cited to evidence that a calcium score represents "the total amount and distribution of calcium within the arteries" (col. 3, lines 63-67), which suggests that the total calcium score provides some indication for the total distribution of plaque and is a supplemental, quantitative measure of overall plaque distribution. Providing a total calcium score, as in the method of Bu et al., does not exclude measure of a distribution of calcified plaque. Additionally, applicant's remarks directed to performing statistical analyses and various mathematical methods are not relevant as these features are not actually claimed.

Applicants acknowledge these statements.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. Claims 1-30 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The Examiner states as follows:

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, claims 1 and 17 have been amended to include "defining an *anatomical distribution* of the areas of calcification..." but this feature is not detailed in applicant's specification.

This rejection is rendered moot as that phrase has been removed from claim 1 and claim 17 has been canceled.

Claim Rejections - 35 USC §103

2. **Claims 1-14, 17-28 and 31-34** stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al. (US 6,233,304) in view of Strauss et al. (US 2002/0115931).

The Examiner states as follows:

Hu et al. disclose a method for detecting coronary artery calcification (CAC) by multi-slice helical reconstruction and/or electron beam computed tomography in a system with arrayed detectors (col. 1, lines 13-15; 42-64). A distribution of calcification is acquired in the form of an attenuation transmission profile (col. 1, lines 19-21), with visualization of data giving rise to mapping sections of arteries or vessels of interest. System components are understood to include data storage and analysis components.

While Hu et al. do not specifically address determining the distribution of calcification, the total calcium score is a general quantitative indicator for both disease risk assessment and plaque distribution within the artery. Additionally, in the same field of endeavor, Strauss et al. teach localizing vascular lesions by characterizing and imaging the distribution of plaque within at the cellular level [0006-7]. The method includes determining the anatomical distribution of plaque, as it is disclosed that the azimuthal distribution is resolved [0007]. It would have been obvious to one of ordinary skill in the art at the time of invention to supplement the calcium score provided in the method of Hu et al. with a characterization of the anatomical distribution of plaque as taught by Strauss et al., in order to accurately resolve stable from vulnerable plaques [0006-7].

The method of Hu et al. includes calculation of x-ray attenuation coefficients in the form of CT numbers that are used in threshold comparison (col. 4, lines 15-36, in which a threshold of 130 HU is selected). The calcium score weighting algorithm for slice spacing correction would include determining changes in calcification density. Hu et al. further disclose plaque density assessment.

- First, Applicants have canceled claims 2-34, amended claim 1, and introduced new claims 35-53. Applicants believe that these amended claims fall within the previously selected invention and apologize for the previous claims being directed to a non-elected invention.

As to the substance of the rejection, Hu et al do not disclose defining a risk score using

anything but calcium density. Strauss et al only describes a method locating localized intravascular lesions. Strauss et al do not teach deriving a risk assessment from the data or from feature and location of the lesions.

The combination of Hu et al and Strauss et al gives rise to a risk assessment based on calcium density and localized intravascular lesions, but the combination does not disclose, teach or even direct an ordinary applicant defining a risk score based on the feature analyzed in the present method – location, heterogeneity, shape, size, texture, and density gradient of each calcified spot in a patient's heart or changes in a location, a heterogeneity, a shape, a size, a texture, and a density gradient of each calcified spot in the patient's heart. Applicants, therefore, respectfully request withdrawal of this rejection.

The Examiner states as follows:

Regarding claim 11, Hu et al. do not explicitly disclose relating calcification densities to an outcome of a lesion; however, Strauss et al. teach that the presence of an atherosclerotic lesion reduces flow through the artery at the site of a lesion, and methods are known to measure this difference [0003]. The image data are presented as pixel density scores and when displayed comprise a transmission profile or map (col. 4, lines 3-55). The progression of plaque is visible from pixel to pixel or from pixel densities across selected regions (col. 4, lines 3-5; 36-51).

This rejection is rendered moot as claim 11 has been canceled. Furthermore, unlike Strauss et al., Naghavi et al. does not claim risk weighting based on flow limiting atherosclerotic lesions. It is well known that flow limitation is not a necessary feature of high risk or vulnerable plaques; in fact, flow limitation is absent in the majority of vulnerable plaques that cause heart attacks.

3. **Claims 12-14, 27 and 28** stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al. (US 6,233,304) in view of Strauss et al. (US 2002/0115931), as applied to claims 1 and 17 above, further in view of Kaufman et al. (US 2003/0095693).

The Examiner states as follows:

Hu as appended by Strauss et al. includes all features of the invention as substantially claimed, including statistical calculation(s), with visualization of data resulting in a map of sections of vessels statistical distribution of calcification of each of a plurality of sections or regions (Hu et al., col. 4, in which a distribution of density scores of pixel values of regions of interest is obtained). Kaufman et al. teach calculation of an average and a range in determination of a peak value [0082]. It would have been obvious to one of ordinary skill in the art at the time of invention to quantify and statistically analyze the calcification data.

This rejection is rendered moot as claims 12-14, 27 and 28 have been canceled. Furthermore, neither Hu et al. nor Kaufman et al. teach that location, shape, texture, density gradient, and heterogeneity of calcified spots add to the risk score.

4. **Claims 15 and 29** are rejected under 35 U.S.C. 103(a) as being unpatentable Hu, Strauss and Kaufman et al., as applied to claims 12-14, 27 and 28, further in view of O'Brien et al. (US 2004/0057955).

The Examiner states as follows:

Hu and Strauss in view of Kaufman et al., as discussed above, includes all features of the invention as substantially claimed and while it can be inferred that a progression of plaque can be visualized in the plaque distribution image, it is not expressly disclosed that progression of plaque is determined; however, O'Brien further teaches a method for treating calcific aortic valve disease [0003-4], including monitoring the calcification and analysis of the progression of plaque. O'Brien further discloses performing statistical analyses on data obtained from scans wherein the progression of the plaque can be observed to evaluate the relationship between progression of plaque and cardiovascular risk factors [0085-86]. It would have been obvious to one of ordinary skill in the art at the time of invention to modify the invention of Hu as appended by Strauss and Kaufman et al. in light of the teachings of O'Brien to include determination of progression of plaque to better characterize risk factors for cardiovascular disease.

This rejection is rendered moot as claims 15 and 29 have been canceled. Furthermore, O'Brien does not teach that changes in shape, texture, density gradient, and heterogeneity of calcified spots add to the risk score.

5. **Claim 16 and 30** stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hu, Strauss, Kaufman and O'Brien et al., as applied to claim 15 and 29 above, further in view of Rather et al. (US 6,385,474).

The Examiner states as follows:

Hu in view of Strauss, Kaufman and O'Brien, as discussed above, substantially disclose all features of the invention as claimed. While Hu et al. disclose categorizing regions according to calcification scores, neither Hu nor Kaufman explicitly disclose categorizing an area of abrupt change in elasticity as a high-risk region. Rather also discloses a method and apparatus for detection and characterization of medical pathologies, such as calcifications, and further teaches studying density and elasticity of the tissue [0013] in which microcalcifications and tissue elasticity are identified [0025]. Regions where there are abrupt changes are identified and each region is classified according to determined criterion [0087]. It would therefore have been obvious to one of ordinary skill in the art at the time of invention to modify that disclosed by Hu in view of Kaufman and O'Brien in light of the teachings of Rather to include ascertaining regions of abrupt changes which assists in the identification of microcalcifications and tissue elasticity which signal pathology such as cancer or calcified plaque.

This rejection is rendered moot as claims 16 and 30 have been canceled. Furthermore, none of Hu, Strauss, Kaufman, O'Brien, or Rather teaches that a very high density plaque (calcification) immediately adjacent to a very low density plaque confer different risk than a gradual decline in the density gradient of a plaque (calcified spot).

Because applicants believe that amended claim 1 and its dependents are fully distinguished from the cited art and believe that new independent claim 43 and its dependents are for the same distinguished from the cited art, Applicant urge that the current claims are allowable over the prior art and urge that is application be passed onto allowance.

If it would be of assistance in resolving any issues in this application, the Examiner is kindly invited to contact applicant's attorney Robert W. Strozier at 713.977.7000

The Commissioner is authorized to charge or credit Deposit Account 501518 for any additional fees or overpayments.

Date: **7 April 2010**

Respectfully submitted,

/Robert W. Strozier/

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